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Case Report

A Case of Facial Diplegia with Paresthesia after Severe Acute Respiratory Syndrome Coronavirus 2 Infection

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ABSTRACT: A 50-year-old man developed dysarthria with dysphagia 14 days after experiencing fever and malaise. He had no upper respiratory symptoms or disturbance of taste or smell. His serum antibodies against severe acute respiratory syndrome coronavirus 2 nucleocapsid phosphoprotein indicated a 73.8 cut-off index (normal value ＜1.0). Contrast-enhanced magnetic resonance imaging revealed enhanced intracranial facial nerves bilaterally. Cerebrospinal fluid examination revealed a cell count of 10/μL (all mononuclear cells), a protein level of 256 mg/dL, and a glucose level of 62 mg/dL. Motor responses of orbicularis oculi muscles by direct facial nerve stimulation were decreased, and bilateral blink reflexes failed to elicit early ipsilateral and late contralateral responses. Nerve conduction study of lower extremities revealed decreased sensory nerve action potential, delayed nerve conduction velocity, and polyphasic F waves. The patient was diagnosed with facial diplegia with paresthesia and dysphagia without anti-ganglioside antibodies. Intravenous gamma globulin therapy was effective for neurological symptoms.

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KEYWORDS: severe acute respiratory syndrome coronavirus 2, facial diplegia with paresthesia, intravenous gamma-globulin therapy

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an enveloped, single-stranded RNA virus that causes human coronavirus disease 2019 (COVID-19), has spread worldwide. The typical symptoms of SARS-CoV-2 infection are fever and respiratory symptoms; however, patients with SARS-CoV-2 infection sometimes develop neurological diseases, such as Guillain-Barré syndrome (GBS).[1,2] Initially, a large-scale cohort study during the early months of the COVID-19 outbreak found no association between COVID-19 and GBS.[3] A subsequent investigation, an international GBS Outcome Study conducted between January 30, 2020 and May 30, 2020,[3] which is a prospective observational cohort study enrolling patients with GBS within two weeks of onset, revealed that patients with GBS caused by SARS-CoV-2 infection frequently had a sensorimotor type GBS and facial palsy. Electrophysiological examination revealed that all patients had a demyelinating peripheral nerve disturbance. Herein, we report the case of a Japanese patient with facial diplegia and paresthesia (FDP)[4] triggered by SARS-CoV-2 infection, who also had a rare combination of symptoms, such as bilateral facial paralysis, dysphagia, and limb

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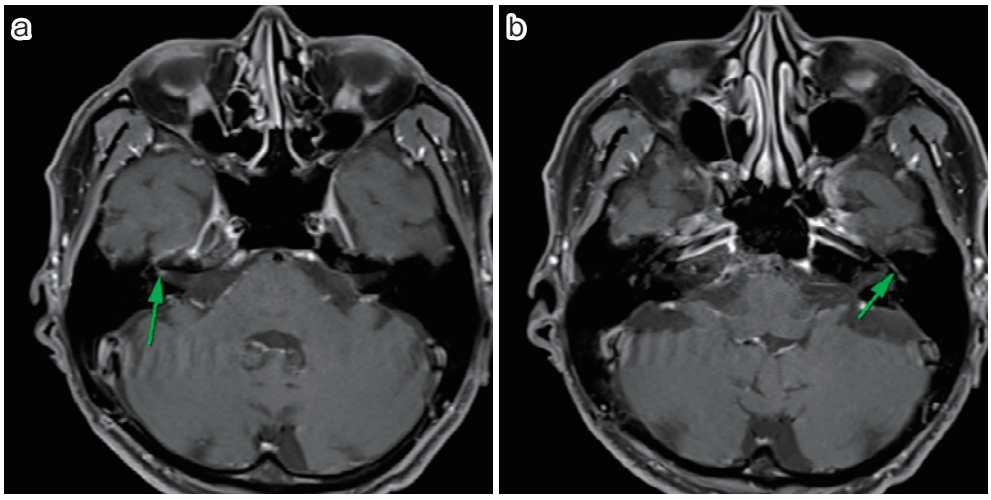

Fig. 1 T1-weighted axial image of brain MRI with contrast enhancement
(a) The green arrow indicates the facial nerve.
(b) The green arrow indicates the left facial nerve out of the internal acoustic foramen.
MRI: magnetic resonance imaging

dysesthesia.

Before writing this manuscript, I informed the patient that I intended to write a paper on his clinical progress and obtained his written consent.

Case Report

A 50-year-old man abruptly developed dysarthria, followed by difficulty in swallowing two days later, and he was admitted to our hospital three days later. He had fever and malaise 14 days before the onset of dysarthria, with no upper respiratory symptoms or disturbance of taste or smell. His primary care physician treated him symptomatically, and his symptoms lasted five days. Despite the SARS-CoV-2 infection outbreak in Japan, testing for SARS-CoV-2 infection was not performed because of the scarcity of respiratory symptoms and disturbance of taste or smell. The patient and his family members or close contacts had no history of SARS-CoV-2 vaccination.

On admission, the patient was afebrile, but he had bilateral peripheral facial nerve palsy, palatal paresis, diffuse hyporeflexia without motor weakness, mild hypesthesia, and paresthesia over his bilateral feet. Fiber laryngoscopy revealed salivary retention in the pyriform fossa but no vocal cord paralysis. Blood tests revealed no abnormalities other than increased platelets (447,000/μL), aspartate transaminase (AST) (39 U/L), and alanine transaminase (ALT) (56 U/L); increased AST and ALT levels might be attributable to fatty liver. Serum immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies against SARS-CoV-2 nucleocapsid phosphoprotein measured using electro-chemiluminescence immunoassay (LSI Medience, Co., Ltd. Tokyo, Japan) were elevated, with a cut-off index of 73.8 (normal value: $<$1.0). However, the patient was not vaccinated with the SARS-CoV-2 vaccine. Chest radiography revealed no pneumonia. Contrast-enhanced cranial magnetic resonance imaging revealed faint enhancement of the bilateral infratemporal part of the facial nerves (Fig. 1). Cerebrospinal fluid (CSF) examination revealed a cell count of 10/μL (all mononuclear cells), a protein level of 256 mg/dL, a glucose level of 62 mg/dL (blood glucose: 96 mg/dL), and an IgG index of 0.68. CSF was cultured for unspecified bacterial species that could grow on chocolate agar medium. Cultures targeting Mycobacterium tuberculosis and fungus were also performed. There was no growth of microorganisms. Viral antibody titers in the CSF were mildly elevated for herpes simplex IgG and mumps IgG (1.59 and 1.73, respectively; normal values: $<$0.2), but the antibody index for varicella-zoster virus was within the normal range (1.4; normal values: $<$ 2.5). Motor responses of the orbicularis oculi muscles by direct facial nerve stimulation were decreased, and bilateral blink reflexes failed to elicit early ipsilateral and late contralateral responses. A nerve conduction study of the lower extremities revealed decreased sensory nerve action potential and delayed nerve conduction velocity, mainly in the sensory nerve of the lower extremities. The F-wave response of the bilateral tibial nerves was polyphasic. These findings suggest mild demyelinating polyneuropathy. Serum anti-

ganglioside antibodies were negative. The patient was diagnosed with FDP and dysphagia. Since FDP has been recognized as a variant of GBS, immune-mediated parainfectious neuropathy was speculated to be an underlying mechanism, and the patient received intravenous gamma globulin therapy (400 mg/kg/day for five days). Three days after starting treatment, the patient's symptoms gradually improved. Within 20 days after the onset of neurological symptoms, the patient became fully asymptomatic.

Discussion

Three pathogeneses are postulated for developing SARS-CoV-2 infection-associated peripheral neuropathies: GBS,[3] GBS variants (pharyngeal-cervical-brachial type,[5] FDP,[6] Miller Fisher syndrome,[3]) and cranial mononeuropathy.[7–9] The first mechanism is direct nervous system invasion by SARS-CoV-2 via blood flow or mucosa of the upper respiratory tract. More than half of the patients infected with SARS-CoV-2 present with olfactory or gustatory disturbances,[10] and many patients with peripheral neuropathy have a simultaneous onset with SARS-CoV-2 infection. The second mechanism is a parainfectious, autoimmune attack against the peripheral nervous system, typically seen in GBS. Many patients with SARS-CoV-2 infection develop GBS approximately 10-14 days after the onset of infection. The third mechanism is the reactivation of the previously infected viruses, such as herpes zoster virus, after SARS-CoV-2 infection. Trigeminal neuropathy with latent herpes zoster[7] or solo facial palsy, the most frequent presentation,[8, 9] may be appropriate examples of this mechanism. In this case, neurological symptoms developed several days after the febrile condition resolved; thus, a parainfectious basis was speculated. Although anti-ganglioside antibodies were negative, the diagnosis of the GBS variant was uncontradicted. GBS diagnosis is based on the patient's history and clinical signs and symptoms.[11] Tests, such as cerebrospinal fluid examination, electrophysiology, and anti-ganglioside antibodies, are adjuncts to diagnosis.[12]

Facial nerve palsy was also reported as a frequent symptom of GBS due to SARS-CoV-2 infection in 42/99 cases (bilateral palsy: 3/99)[13] and 17/44 cases (bilateral palsy: 9/44) in a previous study.[14] Like our case, FDP after SARS-CoV-2 infection is a subtype of GBS with bilateral facial nerve palsy, dysesthesia of the fingertips, and mild weakness, with anti-GD1a IgG/IgM being positive.[6] At the beginning of the SARS-CoV-2 pandemic, many severe COVID-19 cases were reported; however, mild cases and asymptomatic carriers of the virus have now become evident.[12]

In summary, to our knowledge, this is the first reported case of FDP after SARS-CoV-2 infection in Japanese. Clinicians should consider immune-mediated cranial nerve disturbance when they encounter bilateral facial paralysis after a febrile illness, including SARS-CoV-2 infection.

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Authors' contribution: S.K. saw the patient at the first visit and made the diagnosis of his disease and is responsible for this paper. J.I. was the attending physician at the time of admission and treated the patient. M.M. and T.U. helped treat the patients as the supporting physicians. T.U. wrote the manuscript with the main author of this paper on the clinical course. H.K. prepared the MRI picture and described the figure legend. H.S. and T. F. provided advice on the structure of the paper and proofread the paper.

Ethics statement: This study was performed in accordance with the Declaration of Helsinki (1964) and its later amendments. This research protocol was waived from the need for approval under the ethical provisions of the Toho University Medical Center Clinical Research Ethics Committee. The manuscript has been verified by the Toho University School of Medicine Paper Appropriateness Committee to ensure that the appropriate procedures have been followed for submission [Permission no.2021-243]. The patient provided written informed consent to publish this case report and any accompanying images.

Conflicts of interest: None declared.

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